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THE CURE OF HOOKWORM INFECTION.¹

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DURING the recent war there were admitted to the author's gastro-intestinal service at the United States Army General Hospital No. 14, Fort Oglethorpe, Georgia, 393 cases of ankylostomiasis, over one-fourth of which had received previous and obviously unsuccessful hookworm treatment. This large proportion of failures is due, in our opinion, (1) to the real difficulty of achieving a complete cure quickly by the methods of treatment heretofore in vogue, and (2) to the lack of sufficient observation after treatment, owing in turn to the absence of satisfactory scientific data on which the precise criteria of cure could be based. It has been our endeavor to remedy both these defects, the former by the development of the intra-intestinal tube treatment already described² and the latter by means of the most intensive studies of the results of therapy that we could possibly make under army conditions.³

As soon as a hookworm suspect was admitted to our service, and before any treatment was given, stools were sent daily to the laboratory until the diagnosis was confirmed beyond question. After treatment, specimens were similarly examined, every other day, as a rule, until an interval of twenty-eight days had elapsed, unless they were reported positive before that. For the purpose of compiling the statistics presented in this paper, all incomplete observations have been entirely discarded. Our conclusions, accordingly, are based on 231 cases, all of which were observed twenty-nine days or over (up to two hundred and twenty-eight

¹ Read before the Duval County Medical Society, Jacksonville, Fla., Oct. 28, 1919.

² Kantor, J. L.: *The Intra-intestinal Tube Treatment of Hookworm Infection*, *Jour. Am. Med. Assn.*, 1919, vol. lxxiii, 1181.

³ At the time this work was carried on, Lieut.-Col. Calvin D. Cowles, Jr., of the regular army, was in command of the hospital. Dr. Lewis C. Ecker, of Washington, D. C., was in charge of the medical service. Drs. Burrill, Dunning, Paul, Hill, Hughes, Swan, Hagler, Rudbeck and Mahoney were at various times associated with the gastro-intestinal section. Dr. Le Roy Smith was in charge of the laboratory. The actual stool examinations, a task of great magnitude, were very capably performed by Mr. E. A. Piper.

days in one instance), and no case is reported as a cure that did not show an average of ten to fifteen consecutive negative stools during a period of four weeks after treatment. Some of the cured cases we were able to follow for a much longer time, one soldier having his twenty-fourth negative stool one hundred and thirty-six days after treatment.

The first problem that engaged our attention in a preliminary way was the absolute diagnosis of the existence or absence of infection in a given case. Thanks to Kofoid and Barber's loop-flotation-brine method of examining stools for ova,⁴ an extremely delicate laboratory procedure was already at our disposal. We accordingly endeavored to determine how many negative stool examinations should be demanded before a given Southern soldier could be pronounced hookworm-free. Obviously a single examination could not reasonably be expected to reveal every infection either because of errors unavoidable in a large series, because of very slight infections or because the worms were not constantly ovulating. The question was really one of importance not only because we had to be sure of our control methods, but because the reinfection of any case, treated or untreated, had to be taken into consideration. With these objects in mind it was arranged that all Southern soldiers admitted to the *medical* service of the hospital for the period of one month were to have their stools examined five times (on approximately five successive days) or until positive, whereas all patients admitted to the *surgical* service during the same period were to have but a single stool examination. As a result, of the 408 medical cases examined, 63 were found positive after the first stool, 17 more after the second, 12 more after the third and 3 more each after the fourth and fifth—a total of 98 positive cases, or 24 per cent. of the number examined. On the other hand but 32 of the 231 surgical cases were found positive with the single stool method, a percentage slightly under 14. In other words the five-stool method gave an increased incidence of over 9 per cent., and an increased efficiency (as between the two methods) of almost 40 per cent. To crystallize the importance of this, we found that one-quarter of the returning troops were still hookworm-infected by the five-stool method, whereas but one-seventh of the men would have been pronounced positive by a single stool examination.

In this connection it should be stated that the procedure recommended above is designed to reveal infections only in untreated cases or in those whose last treatment took place at least six weeks or two months before the examination. It is of course well known that vermifuges have the property of depressing the egg-laying function of parasites, but the exact duration of this "negative phase" in the case of the female hookworm seems to be a matter of uncertainty.

⁴ Kofoid, C. A., and Barber, M. A.: Rapid Method for the Detection of Ova of Intestinal Parasites in Human Stools, *Jour. Am. Med. Assn.*, 1918, lxxi, 1557.

In order to throw more light on this interesting question an analysis is presented of 100 cases which were reported positive after having received treatment on this service. (See Table I.) The drug used was oil of chenopodium in doses averaging 3. c.c. by tube and 2 c.c.

TABLE I.—SHOWING DAYS ON WHICH STOOLS FIRST BECAME POSITIVE AFTER 100 UNSUCCESSFUL HOOKWORM TREATMENTS.⁵

Days after treatment.	No. of cases positive.	Weekly total percentage.
4	18	1st week, 61
5	19	
6	13	
7	11	
8	3	2d week, 81
9	3	
10	4	
11	1	
12	4	
13	2	
14	2	3d week, 90
15	2	
16	2	
17	1	
18	1	
19	1	
20	2	
21	1	4th week, 98
22	2	
23	2	
24	0	
25	2	
26	1	
27	1	
28	0	
29	0	5th week, 99
30	1	
31	0	
32	0	
33	0	
34	0	
35	0	
36	0	6th week, 100
37	0	
38	0	
39	0	
40	1	

by mouth in capsules. Stools were examined every other day, and in many cases daily, until they came back positive or until an interval of at least four weeks had elapsed after the day of treatment. Since the roentgen ray and other means of studying bowel-emptying have shown that it may take up to seventy-two hours

⁵ Positive results within the first three days are disregarded. See text.

for the complete evacuation of a given meal, an arbitrary three-day limit was established, on the assumption that this would be sufficient for the discharge of all ova produced by worms that had been destroyed by the vermifuge. Accordingly, in the case of stools reported positive within this limit judgment as to cure or failure to cure was suspended until this interval was passed. Subsequently, if the positive results persisted, the case was pronounced uncured; or, if the stools remained negative for *at least four weeks*, the case was called cured. In every instance the period of four weeks was reckoned from the last positive stool, the total observation interval being thus lengthened to thirty-one days when the stool came back positive on the third day after treatment. It will be seen from a study of the accompanying table that observation for four weeks is by no means too long if one wishes to know whether a cure has actually resulted from a given treatment. As it is we have records of 2 cases which became positive only in the fifth and sixth weeks respectively, and by no means all our cases were observed for so long a period. In brief, 98 per cent. of our positive cases (or failures to cure) became such within four weeks, 90 per cent., within three weeks, 80 per cent., within two weeks and only 61 per cent. within the first week. It follows that an individual reported as negative within the first week after treatment may have more than one chance in three of coming back positive at some subsequent examination. That many cases were erroneously considered cured after a routine hookworm treatment as carried out in the various army organizations goes almost without saying. Moreover, when the question of reinfection arises one must be particularly careful that the original disease was actually cured in the first place.

In this connection we should like to point out still another possible source of error in diagnosing the cure of hookworm infection. In their extensive study of this disease in the Orient, Darling, Barber and Hacker⁶ presented a method for grading the value of any particular form of hookworm treatment by comparing the number of worms removed by a first treatment with the total number of worms removed by subsequent treatments. This method was further developed into an "efficiency index" by Knowlton working in Kofoid's service.⁷ Admirable as this procedure is for a comparative study of treatment methods it should by no means be translated into a criterion of cure for the disease, the weak point in the efficiency index method being that further examination of stools presumably ceases as soon as any particular treatment fails to reveal the presence of worms in the excreta. As already explained in the author's previous communication all forms of treatment by mouth have the common objection that the vermifuge is not delivered directly at the site of infection. Hence the chance of

⁶ The Treatment of Hookworm Infection, Jour. Am. Med. Assn., 1918, lxx, 499.

⁷ Knowlton, R. H.: Hookworm Infection among Troops, Ibid., 1919, lxxii, 701.

missing the worms partially or even entirely is by no means merely academic. The following case is cited as an example:

CASE B 208.—Had three treatments, presumably by thymol, before entering the army.

Fourth treatment February 26, 1919, 2 c.c. oil of chenopodium in freshly filled hard, gelatin capsules. *Eighty worms recovered* from resulting stools. Subsequent stools positive for ova for eight days.

Fifth treatment, March 7, same as fourth, *eighteen worms recovered*. Subsequent stools positive on fifth and seventh days.

Sixth treatment, March 18, same as previous, *no worms recovered*. Stools, however, positive on second, third and sixth days.

Seventh treatment, March 27, same as previous *no worms recovered*. Stools positive on second, fourth and sixth days.

Eighth treatment, April 5, same as previous, *twenty worms recovered*. Stools negative for eight days more, at which point observation discontinued. Final result undetermined.

We were again and again impressed with this failure to cure after any of the usual forms of mouth treatment. Indeed, the same conclusion is reached from a study of any of the more careful work that has been reported in the literature. Thus in the severer types of infection encountered by the original Porto Rico Commission⁸ the majority of cases were not cured before four doses of anthelmintic had been administered and there are examples of twenty-two, twenty-three and twenty-five treatments being given without curing the infection. More recently the International Health Board, after a four years' intensive campaign in the West Indies,⁹ is able to report only 50 per cent. of cures after two treatments. Our own experience with the mouth treatment of the relatively mild infections found in the army was not very encouraging. Of the 87 cases treated by the mouth method (2 c.c. oil of chenopodium in freshly filled hard capsules) we could prove a cure in only one-half, this notwithstanding the fact that each man was observed and treated for a period of four weeks or more. If still positive at the end of this observation the patient was either discharged uncured or given tube treatment. As a matter of fact, 5 cases were still positive after six treatments, 3 after seven and 2 were left doubtful (owing to insufficient observation) after eight.

On the other hand our experience with the intra-intestinal tube method convinced us of its superiority over the usual forms of mouth treatment as a means for the rapid and complete eradication of hookworm disease. Of 137 cases treated by the tube we were able to prove a cure, despite the difficulties in observation, in over 87 per cent. Perhaps still more noteworthy is the fact that fully

⁸ Ashford, B. K., and Igaravidez, P. G.: *Uncinariasis in Porto Rico*, Senate Document 808, Washington Government Printing Office, 1911, p. 162.

⁹ Howard, H. H.: *The Control of Hookworm Disease by the Intensive Method*, Publication No. 8, Rockefeller Foundation, New York, 1919, p. 75.

80 per cent. were cured by the first treatment as compared with 34 per cent. by the mouth method. Furthermore, although the mouth method failed in our hands after even a sixth and seventh repetition only one tube case had to go on to a third treatment, the rest being cured in one or two sessions.

TABLE II.—SHOWING COMPARATIVE RESULTS OF MOUTH AND TUBE TREATMENTS.

Treatment.	No. of cases.		Percentage cured separately by each treatment.		Percentage uncured of all cases.	
	Mouth.	Tube.	Mouth.	Tube.	Mouth.	Tube.
1st treatment	35 ¹⁰	137	43	80	86	19.0
2d treatment	70	10	18	90	65	0.7
3d treatment	37	1	32	100	29	0
4th treatment	14	..	21	..	17	
5th treatment	9	..	11	..	9	
6th treatment	5	..	0	..	6	
7th treatment	3	..	0	..	2	
8th treatment	2	..	?	..	?	

It remains to point out still another advantage of the tube technic. It will be observed, by referring again to Table II, that 34 per cent. were cured by taking the first mouth treatment, 18 per cent. by the second, 32 per cent. by the third, 21 per cent. by the fourth, 11 per cent. by the fifth and none at all by the sixth, seventh and eighth. In other words the chances of being cured became progressively less hopeful as treatment was continued. This result is undoubtedly due to errors residing in the rationale of the mouth method, the reason for the fifth failure being just as great as for the first. Such a persistent disappointment might, for example, be due to the patient having achylia gastrica, in which case the associated hypermotility might carry the capsule far into the ileum before its dissolving. On the other hand the soundness of the principle underlying the tube treatment is further vindicated by what might be called its cumulative efficiency, 80 per cent. of the first treatments being successful, 90 per cent. of the second and fully 100 per cent. of the third.

Encouraged by the above experience the author feels justified in recommending the tube method as worthy of trial by the profession. Two treatments, given a week apart, should be sufficient to cure most cases. At first the method should undoubtedly be used only in hospitals, whether civil or military, or in the homes of patients.

¹⁰ Most of the previously *untreated* cases were given tube treatments, hence the relatively small number of first mouth treatments. On the other hand, almost all the previously *treated* cases were given mouth treatments with the exception of a few not included in this table.

After its safety and usefulness are further demonstrated by added experience, and perhaps after appropriate modifications and improvements in the technic, it may not be too much to hope that the tube treatment will ultimately become the method of choice in the eradication of hookworm infection.

SUMMARY. 1. An individual from a hookworm district should not be pronounced hookworm-free until a series of at least five negative stools has been obtained, and then only if the last treatment took place six weeks or more previously.

2. The "latent period" after treatment, *i. e.*, the period in which the egg-laying function of the hookworm is depressed by the vermifuge so that the persistence of worms cannot be revealed by stool examination, may extend up to six weeks. However the great majority (98 per cent.) of cases become positive again within four weeks after treatment.

3. The usual form of treating ankylostomiasis with drugs given by mouth has been shown to be unsatisfactory, even relatively mild infections resisting as many as seven or eight treatments.

4. Much more efficient results can be obtained by the method of intra-intestinal tube treatment, owing to the fact that the full, concentrated dose of vermifuge is delivered precisely at the point of infection. Instead of 34 per cent. of cures, as in the case of a first mouth treatment, fully 80 per cent. are cured by a first tube treatment. Only one repetition is necessary for the relief of the great majority of infections.

THE TREATMENT OF CATARRHAL JAUNDICE BY A RATIONAL, DIRECT AND EFFECTIVE METHOD.¹

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I DESIRE to present in this paper a rational, direct and effective method of treatment of catarrhal jaundice. I say a direct method to draw attention to the contrast between it and the usual symptomatic or expectant plan so commonly employed in treating these cases.

I will limit my subject to the treatment of catarrhal jaundice by this new method, with a passing allusion to the treatment of other more important conditions of the biliary tract.

The diagnosis of catarrhal jaundice, as a rule, does not offer

¹ Read before the Philadelphia Clinical Association October 27, 1919. This is the second of the series of articles on the diagnosis and treatment of diseases of the biliary tract.